REMARKS

Claims 21, 22, and 25-44 are active.

The rejection of Claims 21-23 and 25 under 35 U.S.C. §102(b) over Purton et al are obviated by amendment.

In the outstanding Office Action, the Examiner asserts that Purton et al may have produced osteoclast precursor cells before they obtained osteoclasts. However, contrary to the Examiner's assertion, Purton et al do not disclose a method for producing osteoclast precursor cells because they could not maintain osteoclast precursor cells before differentiating to the osteoclasts. The obtained cells they disclosed were not osteoclast precursor cells, but rather were osteoclasts. For example, their TRAP-positive cells were osteoclasts because those cells are multinucleated (page 1806, col. l, par.3) and they said, "Osteoclasts could also be grown from normal peripheral blood." (page 1807, col. l, par. 2).

In Purton et al, the authors collected non-mobilized PBMCs by leukapheresis etc. Subsequently, the PBMCs were cultured and *non-adherent cells were removed after 3 days culturing* (page 1803, toll, line 4-5). This delay in removal of non-adherent cells accounts for the reason why Purton et al obtained osteoclasts rather than osteoclast precursor cells. In other words, the method disclosed by Purton et al could not stop differentiation of osteoclast precursor cells into osteoclasts, because they did not remove non-adherent cells before 3 days culturing had commenced. Further, the non-adherent cells may produce various cytokines, which can stimulate osteoclast differentiation during 3 days culturing. Therefore, they never obtain osteoclast precursor cells though they can obtain osteoclasts.

On the other hand, in the present application, Applicants obtained osteoclast precursor cells from peripheral blood by removing the non-adherent cells in the early process and then

culturing without any stimulant. Further, Applicants show that the osteoclast precursor cells (the preosteoclasts before the differentiation) had a monocyte like morphology in the testing example on page 19, (1) and Figure. 1). Furthermore, the obtained cells with the presently claimed method are not osteoclasts because the osteoclast precursor cells do not differentiate without any stimulant (for example, IL-3, IL-7, GM-CSF or the like). That is why the stimulation of the cytokines is necessary for the differentiation induction of preosteoclasts into osteoclasts (e.g. page 10, line 6-10). Therefore, the present claimed method represents the first method to obtain osteoclast precursor cells, because this method permits maintaining the osteoclast precursor cells without differentiation to the osteoclasts.

To further underscore the differences between the claimed invention and the method disclosed by Purton et al, Applicants note that in the presently claimed method culturing of the cells is conducted for 1-2 hours before removing the non-adherent cells in RPMI medium to separate non-adherent cells and adherent cells. The non-adherent cells in 1-2 hours culturing did not produce any cytokines, which stimulate osteoclast precursor cells, therefore, osteoclast precursor cells can be obtained. However, in the method of Purton et al, the cells were cultured with non-adherent cells for 3 days. 3 days are sufficiently long enough for the non-adherent cells to produce various cytokines, which stimulate osteoclast differentiation. The foregoing can be readily appreciated by reference to the **attached** Figure comparing the present invention[1] to that disclosed on pages 1802-3 of Purton et al.

In view of the foregoing, Applicants submit that the claimed invention is not anticipated by the disclosure of Purton et al. Accordingly, withdrawal of this ground of rejection is requested.

[1] The present invention is denoted "Our invention (Claim 22)". The designator "Claim 22" corresponds to new Claim 42.

The rejection of Claims 21-25 under 35USC §103(a) over Purton et al taken with Matayoshi et al and Dahl et al is obviated by amendment.

For the reasons set forth above, Purton et al neither disclose nor suggest the present invention. Notably, Purton et al do not disclose the production of osteoclast precursor cells. Further, Purton et al fails to disclose or suggest raising cells in the absence of cytokine(s). Even further, as stated above, one critical difference between the present invention presented in new Claim 42 and the disclosure of Purton et al is that this prior art reference calls for culturing for 3 days as opposed to the claimed culturing time of 1-2 hours.

Moreover, each of Matayoshi et al and Dahl et al discloses a part of the claimed method, but even when viewed together along with he disclosure of Purton et al these references fail to disclose the claimed method of isolating osteoclasts precursor cells from peripheral blood or joint fluid by culturing without any stimulant (i.e., cytokine(s)). Accordingly, Applicants submit that the combined disclosures of Purton et al, Matayoshi et al, and Dahl et al fail to disclose or render obvious the claimed method for obtaining an osteoclast precursor cells without differentiation to an osteoclast.

Accordingly, Applicants request withdrawal of this ground of rejection.

The rejection of Claims 21-25 under 35USC §112, second paragraph, is obviated by the present amendment.

Applicants note that Claim 21 has been amended and new Claim 42 has been added in which they address the Examiner's criticisms. Specifically, the amended and new claims highlight "what cells are cultured" as the cells by the method for producing the same. Further, as for the Examiner's question "what cells are produced" Applicants have clarified

the claims to denote that they are osteoclast precursor cells because all cells except osteoclast precursor cells have died out (Example 1(2) and Example 2(2)).

In view of the present amendments, Applicant request withdrawal of this ground of rejection.

Applicants submit that the present application is in condition for allowance. Early notification to this effect is respectfully requested.

Respectfully submitted,

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